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EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER
1641	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,636	SERTEYN ET AL.	
	Examiner	Art Unit	
	GAILENE R. GABEL	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15 and 17-39* is/are pending in the application.

4a) Of the above claim(s) *24 and 27-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,17-23,25,26 and 32-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *15 and 17-39* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 March 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/2/06; 6/2/08* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Amendment Entry

1. Applicant's preliminary amendment, filed October 28, 2010 is acknowledged and has been entered. Claims 14 and 16 have been cancelled. Claims 15-19, 21, and 23 have been amended. Claims 32-39 have been added. Accordingly, claims 15 and 17-39 are pending.

Election/Restrictions

2. Applicant's election of Group I, claims 15-23, 25, and 26, filed October 28, 2010 is acknowledged and has also been entered. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 24 and 27-31 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. With the addition of claims 32-39, claims 15 and 17-39 are pending. Claims 15, 17-23, 25, 26, and 32-39 are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 15, 17-23, 25, 26, and 32-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15, preamble in line 5, lacks clear antecedent basis in reciting, "the cell activation status." Perhaps, Applicant intends, "the neutrophil cell activation status."

Claim 15 step "1" lacks clear antecedent basis in reciting, "the enzyme" because the preamble appears to recite measuring "the active enzyme content only." Does Applicant intend, "the active enzyme" in step "1"?

Claim 15 is indefinite in being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. In this case, claim 15, step "1" fails to positively recite that the enzyme specific polyclonal or monoclonal antibody is added or contacted with the biological sample in reciting, "via, i.e. using, the enzyme specific polyclonal or monoclonal antibody;" Perhaps, Applicant intends including a step of "adding an enzyme specific polyclonal or monoclonal antibody into the biological sample" prior to the "capturing step."

Claim 15 is also indefinite in being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. In this case, the preamble recites, "A method of measuring the activation status of neutrophil cells in a biological sample obtained from a mammal", whereas, the method steps conclude with "detecting and/or measuring the active enzyme." As such, claim 15 is incomplete in failing to clearly define how the detected and/or measured values of active enzyme

correlate with the activation status of the neutrophil cells. Same analogous comments and problems in claim 15 apply to the “relating step” in claim 21.

Claim 17 is indefinite in failing to provide active positive method steps in reciting the limitations which appear to imply or intend method steps. In this case, “wherein the step of … capturing…, washing step…, then detected by adding …” are not recited as method steps, if "method steps” are intended to further comprise claim 15.

Claim 17 lacks clear antecedent basis in reciting, "the enzyme" in all its occurrences in the claim. Perhaps, Applicant intends, "the active enzyme."

Claim 17 is ambiguous in reciting, “a washing step to remove any components that can interfere with the measurement” because it is unclear what is encompassed by the "components that interfere with measurement”. Does Applicant intend these components to be “unbound components” which are not captured and hence, removed so as to not to interfere with the measurement?

Claim 18 is confusing or has improper antecedent basis problem in relation to claim 17 from which it depends in reciting, “a substrate of fluorimetric reaction product” because claim 17 recites, “a specific substrate to be transformed by the active enzyme.” Accordingly, it is unclear as to whether claims 17 and 18 refer to the same enzyme.

Claim 18 lacks antecedent basis in reciting, "the reaction medium."

Claim 20 has improper antecedent basis problem in reciting, “a neutrophil cell activation status.” Perhaps, Applicant intends “the neutrophil cell activation status.”

Claim 21 lacks clear antecedent basis in reciting, "the enzyme values" it all its occurrences in the claim. Perhaps, Applicant intends, "the active enzyme values."

Claim 21 is vague and indefinite in reciting, "a significant number of healthy mammals" because the terms "significant" and "healthy" are subjective terms that lack a comparative basis for defining their metes and bounds.

Same analogous comments and problems regarding a missing correlation step in claim 15 apply to the “relating step” in claim 21.

Claim 21 lacks clear antecedent basis in reciting, “an activity status of the cells.”

Claim 21 lacks antecedent basis in reciting, “the immunological status.” Additionally, it is unclear what Applicant intends to encompass in reciting, "conditions of the immunological status of the mammals." Please clarify.

Claim 23 is vague and indefinite in reciting, "an effective amount of nitrite" because the term "effective" is subjective term that lacks a comparative basis for defining its metes and bounds.

Claim 25 is indefinite in reciting, "An ELISA kit or device for measuring the activation status of neutrophil cells in a biological sample" because “immunocapturing…” and “detecting and/or measuring…” do not recite structural components of a kit or device. Therefore, it is unclear how claim 25 is an ELISA kit or device. Additionally, the recitation of “comprising the necessary elements for” provides intended use of the unrecited kit or device components in the claim.

Claim 25 is indefinite in reciting, "ELISA." Acronyms or abbreviations should be recited at least one time in a given set of claims.

Claim 26 is indefinite in reciting, "A Specific Immunological Extraction Followed by Enzymatic Detection (SIEFED) kit or device for measuring the activation status of

neutrophil cells in a biological sample" because “immunocapturing…” and “detecting and/or measuring…” do not recite structural components of a kit or device. Therefore, it is unclear how claim 26 is a SIEFED kit or device. Additionally, the recitation of “comprising the necessary elements for” provides intended use of the unrecited kit or device components in the claim.

Claim 32 lacks clear antecedent basis in reciting, "the enzyme." Perhaps, Applicant intends, "the active enzyme."

Claim 33 lacks clear antecedent basis in reciting, "the enzyme." Perhaps, Applicant intends, "the active enzyme."

Claim 34 lacks clear antecedent basis in reciting, "the enzyme." Perhaps, Applicant intends, "the active enzyme."

Claim 36 lacks clear antecedent basis in reciting, "quantifying enzyme level." Perhaps, Applicant intends, "quantifying the active enzyme level." It is further confusing what Applicant intends to encompass in reciting, “quantifying enzyme level with a standard enzyme curve.” Does Applicant perhaps intend “comparing and correlating the quantified active enzyme level with predetermined active enzyme standard curve.”

Claim 37 lacks clear antecedent basis in reciting, "the enzyme." Perhaps, Applicant intends, "the active enzyme."

Claim 38 lacks clear antecedent basis in reciting, "the enzyme." Perhaps, Applicant intends, "the active enzyme."

Claim 39 lacks clear antecedent basis in reciting, "the enzyme." Perhaps, Applicant intends, "the active enzyme."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 25, 26, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Deby et al. (US Patent 5,460,961).

Deby et al. disclose immunological detection of recombinant myeloperoxidase (MPO) and its enzyme activity using an enzyme-linked immunosorbent assay (ELISA) system (device or kit). In using the ELISA kit, cell culture supernatant containing the MPO is first contacted with active enzyme-specific antibody to MPO adsorbed onto 96-microwell tray so as to capture the active enzyme/MPO. After the contacting/capturing step, a washing step is performed to remove unbound components which may interfere with the measurement of the enzyme activity. The active MPO-specific antibody may be either monoclonal or polyclonal antibody. The presence and/or amount of the recombinant MPO is detected and measured using a chromogenic substrate (paranitrophenyl phosphate). The enzyme activity of the MPO is also assayed using O-dianisidine or orthophenylene diamine as substrate in the presence of hydrogen peroxide in the reaction mixture. Deby et al. teach that an effective amount of nitrite in the form of sodium salt or any other form of earth alkali salt is also added into the

reaction mixture (MgCl, NaCl) in obtaining the generation of an enhanced signal (col. 21, line 36 to col. 22, line 6).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 15, 17-21, 23, 32, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hansel et al. (WO 99/61907) in view of Deby et al. (US Patent 5,460,961).

Hansel et al. disclose a method for measuring activation status of neutrophils (PMNs or polymorphonuclear cells) in a biological sample (Abstract; p. 1, lines 3-8). The biological sample may be cellular or acellular such as venous or capillary blood,

sputum, nasal fluids, and tissue cells (p. 10, lines 21-24). The biological sample (blood) is obtained from a mammal and contains leucocyte subpopulations such as neutrophil cells and/or active enzyme released from neutrophil cells. Hansel et al. teach that the active enzyme released by the neutrophils is MPO (Abstract; p. 1, 21-28; p. 2, lines 17-23). Hansel et al. provide that the method differentially measures active MPO enzyme content only released by neutrophils, the enzyme content being correlated with the neutrophil/cell activation status as shown in page 4, lines 5-7, page 6, lines 12-14, and page 7, lines 1-3. In the method, Hansel et al. teach contacting the active enzyme with hydrogen peroxide as a specific substrate and a chromogen which is transformed by the active enzyme into a visible fluorimetric reaction product (p. 1, lines 9-14; p. 3, lines 7-9; p. 11, lines 21-22). The neutrophil activation status is then measured and correlated to a disease or pathological condition (Abstract). Correlation is performed by comparing the active enzyme content values with normal control samples having normal active enzyme levels from healthy subjects or mammals (p. 1, lines 21-28; p. 2, lines 10-15). Hansel et al. also disclose a ELISA kit or device (p. 2, lines 25-27).

Hansel et al. differ from the instant invention in failing to teach contacting the biological sample with polyclonal or monoclonal antibody that is specific for the active enzyme MPO so as to specifically capture the active enzyme MPO.

Deby et al. disclose immunological detection of recombinant MPO and its enzyme activity using an ELISA system (device or kit). Cell culture supernatant containing the MPO is first contacted with active enzyme-specific antibody to MPO adsorbed onto 96-microwell tray so as to capture the active enzyme/MPO. After the

contacting/capturing step, a washing step is performed to remove unbound components which may interfere with the measurement of the enzyme activity. Deby et al. teach that the active MPO-specific antibody may be either monoclonal or polyclonal antibody. Thereafter, the presence and/or amount of the recombinant MPO is detected and measured using a chromogenic substrate (paranitrophenyl phosphate). The enzyme activity of the MPO is also assayed using O-dianisidine or orthophenylene diamine as substrate in the presence of hydrogen peroxide in the reaction mixture. An effective amount of nitrite in the form of sodium salt or any other form of earth alkali salt is also added into the reaction mixture (MgCl, NaCl) in obtaining the generation of an enhanced signal (col. 21, line 36 to col. 22, line 6).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the immunological detection method taught by Deby which utilizes polyclonal and monoclonal antibodies that specifically bind MPO into the method of Hansel which differentially detects for concentration and activity of active enzymes in neutrophils such as MPO, because Deby specifically taught that such the antibodies can be used in immunological enzyme assay methods to specifically capture and detect levels and activity of MPO such as those released by neutrophils in the method of Hansel.

6. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hansel et al. (WO 99/61907) in view of Deby et al. (US Patent 5,460,961) as applied to claims 15, 17-21, 23, 32, and 36 above, and in further view of Deby-Dupont et al. (Equine

Neutrophil Myeloperoxidase in Plasma: design of a radio-immunoassay and first results in septic pathologies, Veterinary Immunology and Immunopathology 66: 257-271 (1998)).

Hansel et al. and Deby et al. are discussed supra. Hansel et al. and Deby et al. differ from the instant invention in failing to teach that the mammal is a horse.

Deby-Dupont et al. teach obtaining specific antiserum against MPO and immunologically assaying for the presence and amount of MPO in horses and determining pathological conditions such as strangulation intestinal pathologies which are accompanied by local activation of neutrophils. Such conditions can be revealed by measuring tissular enzymatic activity of the granulocytic enzyme: MPO using the specific antibody (antiserum) to MPO (Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to immunologically assay for the amount and activity of MPO as taught by Hansel as modified by Deby, in a blood sample obtained from a horse as taught by Deby-Dupont because Hansel and Deby specifically taught that polyclonal and monoclonal antibodies can be used in immunological enzyme assay methods to specifically capture and detect accurate levels and activity of MPO from neutrophils and Deby-Dupont expressly showed the significance of specifically measuring accurate level and activity of MPO in determining conditions such as strangulation intestinal pathologies in horses which occurs by local activation of neutrophils.

7. Claims 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deby et al. (US Patent 5,460,961) in view of Terao et al. (US Patent 5,290,679).

Deby et al. is discussed supra. Deby et al. differ from the instant invention in failing to teach that the active enzyme may be any one of elastase or trypsin.

Terao et al. teach that elastase and trypsin are granulocyte enzymes that are also released by neutrophil cells, the concentrations and enzyme activities of which are also measured immunologically. Terao et al. specifically teach measuring elastase using anti-elastase antibody conjugated to enzyme labels (Example 6 and Example 7).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to immunologically detect and measure levels and activity of other enzymes such as elastase and trypsin as taught by Terao using polyclonal or monoclonal anti-elastase antibodies and anti-trypsin antibodies in immunological enzyme assays such as applied with MPO as taught by Deby because elastase and trypsin appear to be obvious variations of other active enzymes released by subpopulations of leucocytes including neutrophils when activated, as in the method of Deby.

8. Claims 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hansel et al. (WO 99/61907) in view of Deby et al. (US Patent 5,460,961) as applied to claims 15, 17-21, 23, 32, and 36 above, and in further view of Terao et al. (US Patent 5,290,679).

Hansel et al. and Deby et al. are discussed supra. Hansel et al. and Deby et al. differ from the instant invention in failing to teach that the active enzyme may be any one of elastase or trypsin.

Terao et al. is discussed supra.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to immunologically detect and measure levels and activity of other enzymes such as elastase and trypsin as taught by Terao using polyclonal or monoclonal anti-elastase antibodies and anti-trypsin antibodies in immunological enzyme assays such as applied with MPO as taught by Hansel as modified by Deby because elastase and trypsin appear to be obvious variations of other active enzymes released by subpopulations of leucocytes including neutrophils when activated, as in the method of Hansel and Deby.

9. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hansel et al. (WO 99/61907) in view of Deby et al. (US Patent 5,460,961) as applied to claims 15, 17-21, 23, 32, and 36 above, and in further view of Wilson et al. (US 2006/0257879).

Hansel et al. and Deby et al. are discussed supra. Hansel et al. and Deby et al. differ from the instant invention in failing to teach a substrate which is 10-acetyl-3,7-dihydroxyphenoxazine.

Wilson et al. teach that peroxidase activity is present in many cells and that many fluorogenic substrates for horseradish peroxidase are well known in the art and are

commercially available in ELISA kits and systems. Wilson et al. specifically teach that 10-acetyl-3,7-dihydroxyphenoxazine is a well-known fluorogenic substrate which is advantageous for its ability to react with hydrogen peroxide in the presence of horseradish peroxidase and produce highly fluorescent resolution signal.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate 10-acetyl-3,7-dihydroxyphenoxazine as a fluorogenic substrate into the method of Hansel and Deby in immunologically detecting and measuring levels and activity of MPO because 10-acetyl-3,7-dihydroxyphenoxazine appears to be an obvious variation of fluorogenic substrate known and used in immunological enzyme assay methods such as taught by both of Hansel and Deby, which is advantageous for its ability to produce highly fluorescent resolution signal.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GAILENE R. GABEL whose telephone number is (571)272-0820. The examiner can normally be reached on Monday, Tuesday, Thursday, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GAILENE R. GABEL/
Primary Examiner, Art Unit 1641

November 6, 2010